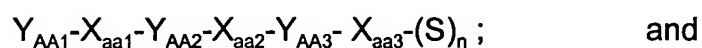
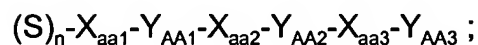
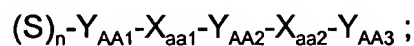
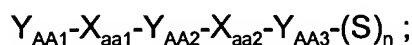
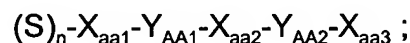
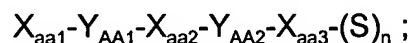
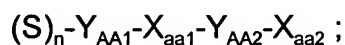
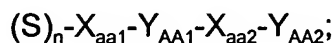
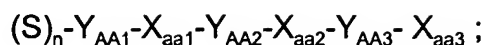


We claim:

1 1. A compound for inhibiting the toxicity of an amyloid protein or amyloid
2 peptide, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing
3 sequence of at least four modified or unmodified amino acids; said compound comprising
4 a peptidyl sequence selected from the group consisting of:





wherein:

(a) X_{aa1} , X_{aa2} , and X_{aa3} are natural or synthetic amino acids that are identical or homologous to alternating amino acids of the aggregation-inducing sequence of the amyloid protein or amyloid peptide, and that have side chains adapted for cross-strand side chain interactions with a β -sheet;

(b) Y_{AA1} , Y_{AA2} , and Y_{AA3} are natural or synthetic amino acids that are identical or homologous to alternating amino acids of the aggregation-inducing sequence of the amyloid protein or amyloid peptide; wherein Y_{AA1} , Y_{AA2} , and Y_{AA3} correspond to amino acids that will be positioned on opposite faces of a β -sheet containing the amino acids that correspond to X_{aa1} , X_{aa2} , and X_{aa3} ; and wherein the amino acids in the amyloid protein or amyloid peptide that correspond to X_{aa1} , X_{aa2} , and X_{aa3} alternate with the amino acids in the amyloid protein or amyloid peptide that correspond to Y_{AA1} , Y_{AA2} , and Y_{AA3} ; wherein at least one of Y_{AA1} , Y_{AA2} , and Y_{AA3} is a C $^{\alpha,\alpha}$ -disubstituted amino acid;

(c) $(S)_n$ is a hydrophilic region comprising hydrophilic amino acids or other hydrophilic groups; wherein $(S)_n$ consists of from 0 to 10 amino acids, or otherwise has a size not larger than about the size of a decapeptide;

(d) either or both ends of said peptidyl sequence optionally comprise additional functionality that does not adversely affect the compound's ability to inhibit the toxicity of an amyloid protein or amyloid peptide, as compared to an otherwise identical compound lacking such additional functionality; and

56 **(e)** the number of amino acids in the aggregation sequence of the amyloid protein
57 or amyloid peptide may be the same as, or different from, the number of natural or
58 synthetic amino acids in said peptidyl sequence.

1 **2.** The compound of Claim 1, wherein said compound is selected from the
2 group consisting of Lys-Dibg-Val-Dbzg-Phe-Dpg-(Lys)₆-NH₂ (SEQ ID NO: 4); (Lys)₇-Dibg-
3 Val-Dbzg-Phe-Dpg-NH₂ (SEQ ID NO: 5); Lys-Dibg-Val-Dbzg-Phe-Dpg-Lys-NH₂ (SEQ ID
4 NO: 6); and Lys-Dibg-Val-Dbzg-Phe-Dpg-NH₂ (SEQ ID NO: 7).

1 **3.** The compound of Claim 2, wherein said compound is Lys-Dibg-Val-Dbzg-
2 Phe-Dpg-(Lys)₆-NH₂ (SEQ ID NO: 4).

1 **4.** The compound of Claim 2, wherein said compound is (Lys)₇-Dibg-Val-Dbzg-
2 Phe-Dpg-NH₂ (SEQ ID NO: 5).

1 **5.** The compound of Claim 2, wherein said compound is Lys-Dibg-Val-Dbzg-
2 Phe-Dpg-Lys-NH₂ (SEQ ID NO: 6).

1 **6.** The compound of Claim 2, wherein said compound is Lys-Dibg-Val-Dbzg-
2 Phe-Dpg-NH₂ (SEQ ID NO: 7).

1 **7.** The compound of Claim 1, wherein the aggregation-inducing sequence is
2 selected from the group consisting of KLVFFA (SEQ ID NO: 3); FLVHS (SEQ ID NO: 9);
3 NFLVH (SEQ ID NO: 10); NFGAIL (SEQ ID NO: 11); VGGAVVTGV (SEQ ID NO: 12);
4 VNITIKQHTVTTTT (SEQ ID NO: 13); LANFLV (SEQ ID NO: 14); FLVHSS (SEQ ID NO:
5 15); AGDV (SEQ ID NO: 16); and Q_m; wherein *m* is an integer from 25 to 45.

1 **8.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 KLVFFA (SEQ ID NO: 3).

1 **9.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 FLVHS (SEQ ID NO: 9).

1 **10.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 NFLVH (SEQ ID NO: 10).

1 **11.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 NFGAIL (SEQ ID NO: 11).

1 **12.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 VGGAVVTGV (SEQ ID NO: 12).

1 **13.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 GAV.

1 **14.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 VNITIKQHTVTTTT (SEQ ID NO: 13).

1 **15.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 LANFLV (SEQ ID NO: 14).

1 **16.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 FLVHSS (SEQ ID NO: 15).

1 **17.** The compound of Claim 7, wherein the aggregation-inducing sequence is
2 AGDV (SEQ ID NO: 16).

1 **18.** The compound of Claim 7, wherein the aggregation-inducing sequence is Q_m ;
2 wherein m is an integer from 25 to 45.

1 **19.** The compound of Claim 1, wherein at least two of Y_{AA1} , Y_{AA2} , and Y_{AA3} are $C^{\alpha,\alpha}$ -
2 disubstituted amino acids.

1 **20.** The compound of Claim 1, wherein each of Y_{AA1} , Y_{AA2} , and Y_{AA3} is an $C^{\alpha,\alpha}$ -
2 disubstituted amino acids.

1 **21.** A composition of matter comprising the compound of Claim 1, and a
2 pharmaceutically acceptable carrier.

1 **22.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 1.

1 **23.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 2.

1 **24.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 3.

1 **25.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 4.

1 **26.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 5.

1 **27.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 6.

1 **28.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 7.

1 **29.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 8.

1 **30.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 9.

1 **31.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 10.

1 **32.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 11.

1 **33.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 12.

1 **34.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 13.

1 **35.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 14.

1 **36.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 15.

1 **37.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 16.

1 **38.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 17.

1 **39.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 18.

1 **40.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 19.

1 **41.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the compound of Claim 20.

1 **42.** A method for inhibiting the toxicity of an amyloid protein or amyloid peptide
2 in a mammal, said method comprising administering to the mammal an effective amount
3 of the composition of Claim 21.

1 **43.** The method of Claim 22, wherein the compound promotes the aggregation
2 of an amyloid protein or amyloid peptide into a non-toxic, non-fibril conformation.

1 **44.** The method of Claim 22, wherein the compound causes a reduction in the
2 concentration of protofibrils formed from an amyloid protein or amyloid peptide.

1 **45.** The method of Claim 22, wherein the compound causes dissolution of fibrils
2 of the amyloid protein or amyloid peptide.

1 **46.** The method of Claim 22, wherein the method is used to prevent or inhibit a
2 disease associated with amyloid plaque.

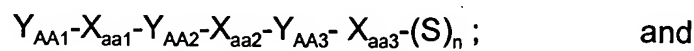
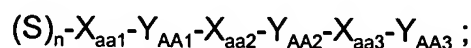
1 **47.** The method of Claim 22, wherein the method is used to prevent or inhibit a
2 disease selected from the group consisting of Alzheimer's disease, Parkinson's disease,
3 Creutzfeld-Jacob Disease, hemodialysis-associated amyloidosis, Type II diabetes, age-
4 associated cardiac dysfunction, early-onset Alzheimer's disease, early-onset Parkinson's
5 disease, Huntington's Disease, Familial Creutzfeld-Jacob disease, fatal familial insomnia,
6 Gerstmann-Straussler-Scheinker disease, hereditary cerebral amyloid angiopathy, primary
7 systemic amyloidosis, secondary systemic amyloidosis, Portuguese-type familial amyloid
8 polyneuropathy, ApoA1 associated familial amyloid polyneuropathy, Finnish type familial
9 amyloid polyneuropathy, hereditary systemic amyloidosis, prolactinoma of the pituitary, and
10 transferable spongiform encephalopathies.

1 **48.** The method of Claim 22, wherein the method is used to prevent or inhibit
2 Alzheimer's disease.

1 **49.** The method of Claim 22, wherein the method is used to prevent or inhibit
2 Parkinson's disease.

1 **50.** The method of Claim 22, wherein the method is used to prevent or inhibit
2 Type II diabetes.

51. A compound as recited in Claim 1, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least six modified or unmodified amino acids, and wherein said peptidyl sequence is selected from the group consisting of:



52. A compound as recited in Claim 1, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least five modified or unmodified amino acids, and wherein said peptidyl sequence is selected from the group consisting of:

